REMARKS

Amendments to the Specification

The specification is amended to delete hypertext links and correct trademark usage.

Amendments to the claims

Claim 94's recitation that the peptide is isolated is supported throughout the specification; at page 29, line 3 to page 31, line 33, for example. Claim 96's recitation of a transmembrane domain is supported, *inter alia*, at page 29, lines 22-24. Claim 114 is amended to depend from claim 23. Claim 2 is amended to correct a clerical error. New claims 127 and 128 are supported, *inter alia*, at page 297, line 21 to page 299, line 1. New claims 129-132 are supported, *inter alia*, at page 30, line 1 to page 31, lines 15-25.

Claim Objections

Claim 96 and 122 stand objected for informalities. Claim 96 is amended to recite a transmembrane domain region and claim 122 is now withdrawn.

Applicants respectfully request withdrawal of the objections.

Rejection Under 35 U.S.C. § 101

Claims 94-98 stand rejected as directed to non-statutory subject matter. Claim 94 is amended to recite an isolated polypeptide. Claims 95-98 depend from claim 94. The claims are no longer directed to products of nature.

Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 112

Claims 22, 23, 25-28, 114, 115, and 117 stand rejected as not enabled because undue experimentation would be required to develop a SARS vaccine.

Applicants respectfully traverse the rejection.

A patent specification must teach a person skilled in the relevant art how to make and use the invention claimed. 35 U.S.C. § 112 ¶ 1. The legal test for whether a disclosure provides adequate enablement for a generic claim is that "the scope of the claims must bear a *reasonable correlation* to the scope of enablement provided by the specification to persons of ordinary skill in the art." *In re Fisher*, 427 F.2d 833, 839, 166 U.S.P.Q. 18, 24 (C.C.P.A. 1970) (emphasis added), *cited with approval in Amgen, Inc. v. Chugai Pharmaceutical Co.*, 927 F.2d 1200, 1212, 18 U.S.P.Q.2d 1016, 1026 (Fed. Cir. 1991). The standard for determining whether the present specification meets the enablement requirement is whether any experimentation which may be needed to practice the invention is undue. *In re Wands*, 858 F.2d 731, 736-37 (Fed. Cir. 1988). Even complex experimentation may not be considered undue if the art typically engages in such experimentation. *In re Certain Limited-Charge Cell Culture Microcarriers*, 221 U.S.P.Q. 1165, 1174 (Int'l Trade Comm'n 1983), *aff'd. sub nom., Massachusetts Institute of Technology v. A.B. Fortia*, 774, F.2d 1104 (Fed. Cir. 1985). A patent need not teach, and preferably omits, what is well known in the art. *In re Buchner*, 929 F.2d 660, 661, (Fed. Cir. 1991); *Hybritech, Inc. v. Monoclonal Antibodies, Inc.*, 802 F.2d 1367, 1384, (Fed. Cir. 1986), *cert. denied*, 480 U.S. 947 (1987); and *Lindemann Maschinenfabrik GMBH v. American Hoist & Derrick Co.*, 730 F.2d 1452, 1463 (Fed. Cir. 1984).

The Office Action at page 6 acknowledges that the specification discloses how to makes polypeptides and subunit S polypeptides. The Office Action also acknowledges

that Examples 4 and 5 of the specification teach that inactivated SARS vaccine can induce neutralizing antibodies in mice and Balb/c mice. *Id.* Nevertheless, the Office Action contends, citing Weiss,[1] that the "mice model is not [an] art-recognized animal model for assessing SARS infection." *Id.*

Whether an animal model accurately reproduces a disease etiology is not the test of whether the animal model correlates to the condition. Citing *In re Brana*, 51. F.3d 1560, 1566 (Fed. Cir. 1995), the M.P.E.P. explains that:

> ...[i]f the art is such that a particular model is recognized as correlating to a specific condition, then it should be accepted as correlating unless the examiner has evidence that the model does not correlate.

M.P.E.P § 2164.02. Thus, a rigorous or invariable exact correlation is not required. *Cross. v. Iisuka*, 753 F.2d 1040 (Fed. Cir. 1985).

Weiss may teach that the mouse is not a perfect model for understanding SARS *pathology*; however, Weiss demonstrates clearly that the art recognizes, and continues to use, mice models to test SARS vaccines. Weiss acknowledges issues using animal models for SARS disease. See page 653, col.2 ¶ 3. But Weiss recognizes that mice models are used for testing SARS vaccines: "It should be emphasized that these animals (in particular mice and macaques) are currently being exploited for vaccine studies." Page 653, col.2 ¶ 3. Weiss also describes multiple SARS vaccine studies using experiments performed in mice, including at least one study demonstrating protection from SARS: "[A] DNA vaccine encoding the codon-optimized SARS spike glycoprotein induces neutralizing antibody as well as T-cell responses. Protection from SARS-CoV challenge was mediated by a humoral immune response but not by a T-cell dependent

[1] Weiss SR, Navas-Martin S. "Coronavirus pathogenesis and the emerging pathogen severe acute respiratory syndrome coronavirus," Microbiol Mol Biol Rev. 2005 Dec;69(4):635-64. Weiss was published after Applicants' filing date.

mechanism." See Page 654, col.1 ¶ 3. Thus, Weiss recognizes that the mouse model is art-recognized for SARS vaccine research.

The Office Action also considers the claims lack enablement because "the molecular biology and pathogenesis of SARS-HCoV were largely unknown" and, citing Stockman,[2] because "the prior art indicates that no drug or treatment has been proven to be effective for control of SARS." Office Action at page 7. Neither rationale supports a lack of enablement. First, vaccine development does not require that the molecular biology and pathogenesis of SARS virus is known. Indeed, as discussed above, the skilled artisan performs vaccine studies in mice, which may not be a good model for understanding either SARS virus molecular biology or pathology, but is useful in vaccine research. Second, Stockman describes the failure of ribavirin, lopinavir, corticosteroids, interferon, intravenous immunoglobulin and convalescent plasma to treat SARS. However, Stockman teaches nothing about vaccine-based treatments using the host's immune system. Thus, nothing in Stockman suggests that Applicants claimed subject matter is not enabled.

Finally, the Office action suggests that if SARS virus reemerges in humans, its spike protein might not be the same and thus Applicants' vaccine might not be effective. Office Action at page 7. This is speculation based on Cavanagh's statement that the "S1 protein might not be the same as that of the 2002/2003 outbreak. Research with IBV [Infectious Bronchitis Virus] has indicated that differences of only 5% of S1 protein amino acid can reduce cross-protection." Page 577, col.2 ¶ 4. But nothing in Cavanagh shows that Applicants vaccine will not protect against a hypothetical future SARS

[2] Stockman LJ, Bellamy R, Garner P., "SARS: systematic review of treatment effects," PLoS Med. 2006 Sep;3(9):e343

variant. Indeed, there is nothing in Cavanagh to suggest that that SARS virus even mutates as IBV does. IBV is a type 3 coronavirus and SARS virus has been classed as a Group 4 coronavirus because of "extremely low amino acid identity between its proteins and those of the other three groups, and [the] nature and organization of its non-structural protein genes." Page 568, col.2. Table 1 legend. Finally, rather than suggesting that the S1 protein will not be useful as a vaccine, Cavanagh *encourages* using the S1 protein in SARS vaccines: "Looking further into the future, the high efficacy of the fowl adenovirus vector expressing the IBV S1 subunit provides optimism for a live SARS vaccine." Abstract, p.568. Nothing in Cavanagh provides any reason to doubt Applicants' claims are enabled.

The experimentation required to develop a SARS vaccine may be complex but it is not undue. The specification provides detailed instructions how to prepare spike glycoprotein; how to perform the mouse experiments; and provides examples with inactivated virus detailing the neutralizing antibody response obtained in mice, an accepted model for identifying SARS vaccines. Weiss demonstrates that Applicants' disclosed experiments are regularly performed in the art. The weight of the evidence establishes that claims 22, 23, 25-28, 114, 115, and 117 are enabled. The Office Action has not established a *prima facie* case to the contrary.

Applicants respectfully request withdrawal of the rejection.

Rejection Under 35 U.S.C. § 102

Claims 1-8, 22, 23, 27, 28, and 94 stand rejected under 35 U.S.C. § 102(e) as anticipated by Plummer (US2007/0258999) as evidenced by Dimitrov

(US2006/0240515A1).

Applicants respectfully traverse the rejection.

Plummer's spike protein sequence is not prior art to Applicants spike sequence because Applicants were in possession of Plummer's disclosed Spike sequence prior to Plummer's filing date. See *In re Stempel*, 241 F.2d 755, 759 (CCPA 1957)(Holding that "all the applicant can be required to show is priority with respect to so much of the claimed invention as the reference happens to show. When he has done that he has disposed of the reference.")

Plummer's only disclosed Spike sequence is SEQ ID NO:33, which is identical to Applicants SEQ ID NO:6042. Applicants claim priority to U.S. provisional application No. 60/463109, filed April 14, 2003. SEQ ID NO:147[3] in Application No. 60/463109 discloses the identical sequence to SEQ ID NO:6042. Applicants' invention thus pre-dates Plummer, which has an earliest possible filing date of April 28, 2003. Thus, while the sequence identifier "6042" may have been used for the first time in Application Serial No. 60/51781, filed October 11, 2003 (noted at page 3 of the Office Action), the sequence itself was first disclosed as sequence identifier 147 in Application Serial 60/463109, filed April 14, 2003. Plummer is therefore not prior art to SEQ ID NO:6042 or SEQ ID NO:7307.

Applicants respectfully request withdrawal of the rejection.

Rejections Under 35 U.S.C. § 103(a)

Claims 95-98 stand rejected under 35 U.S.C. § 103(a) as obvious over Plummer

[3] Copies of Provisional Application 60/463,109 pages 42 to 48, which disclose SEQ ID NO:6042 as SEQ ID: 147, are enclosed as Exhibit 1 for the Examiner's convenience.

and Cavanagh *et al.* (J. Gen. Virol. 1986 67:1435-42; "Cavanagh"). Claims 25, 26, 114, 115, and 117 stand rejected under 35 U.S.C. § 103(a) as obvious over Plummer and Gasparini *et al.* (Eu. J. Epidemiol. 2001 17:135-140; "Gasparini.")

Plummer is cited as teaching SEQ ID NO:33, the Spike protein, prior to Applicant's priority date. As discussed above, Plummer's teaching of SEQ ID NO:33 is not prior art to SEQ ID NO:6042 or SEQ ID NO:7307. Neither Cavanagh nor Gasparini cures the deficiency of Plummer. The Office Action has not established a *prima facie* case of obviousness.

Applicants respectfully request withdrawal of the rejection.

Respectfully submitted,

BANNER & WITCOFF, LTD.

Dated: Feb 20,2009
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The invention includes a polypeptide comprising an amino acid sequence having sequence identity to SEQ ID NO: 146. The invention includes a fragment of a polypeptide comprising SEQ ID NO: 146. The invention includes a diagnostic kit comprising a polypeptide comprising SEQ ID NO: 146, or a fragment thereof. The invention includes a diagnostic kit comprising a polynucleotide sequence encoding SEQ ID NO: 146, or a fragment thereof. The invention includes an immunogenic composition comprising a polypeptide comprising SEQ ID NO: 146, or a fragment thereof. The invention includes an antibody which recognizes a polypeptide comprising SEQ ID NO: 146, or a fragment thereof.

SEQ ID NO: 146 also contains an open reading frame comprising SEQ ID NO: 147. The invention includes a polypeptide comprising SEQ ID NO: 147. SEQ ID NO: 147 is set forth below.

SEQ ID NO: 147

MFIFLLFLTLTSGSDLDRCTTFDDVQAPNYTQHTSSMRGVYYPDEIFRSDTLYLTQDLFLP
FYSNVTGFHTINHTFGNPVIPFKDGIYFAATEKSNVVRGWVFGSTMNNKSQSVIIINNSTN
VVIRACNFELCDNPFFAVSKPMGTQTHTMIFDNAFNCTFEYISDAFSLDVSEKSGNFKHL
REFVFKNKDGFLYVYKGYQPIDVVRDLPSGFNTLKPIFKLPLGINITNFRAILTAFSPAQDI
WGTSAAAYFVGYLKPTTFMLKYDENGTITDAVDCSQNPLAELKCSVKSFEIDKGIYQTS
NFRVVPSGDVVRFPNITNLCPFGEVFNATKFPSVYAWERKKISNCVADYSVLYNSTFFST
FKCYGVSATKLNDLCFSNVYADSFVVKGDDVRQIAPGQTGVIADYNYKLPDDFMGCVL
AWNTRNIDATSTGNYNYKYRYLRHGKLRPFERDISNVPFSPDGKPCTPPALNCYWPLND
YGFYTTTGIGYQPYRVVVLSFELLNAPATVCGPKLSTDLIKNQCVNFNFNGLTGTGVLTP
SSKRFQPFQQFGRDVSDFTDSVRDPKTSEILDISPCAFGGVSVITPGTNASSEVAVLYQDV
NCTDVSTAIHADQLTPAWRIYSTGNNVFQTQAGCLIGAEHVDTSYECDIPIGAGICASYH
TVSLLRSTSQKSIVAYTMSLGADSSIAYSNNTIAIPTNFSISITTEVMPVSMAKTSVDCNMY
ICGDSTECANLLLQYGSFCTQLNRALSGIAAEQDRNTREVFAQVKQMYKTPTLKYFGGF
NFSQILPDPLKPTKRSFIEDLLFNKVTLADAGFMKQYGECLGDINARDLICAQKFNGLTVL
PPLLTDDMIAAYTAALVSGTATAGWTFGAGAALQIPFAMQMAYRFNGIGVTQNVLYEN
QKQIANQFNKAISQIQESLTTTSTALGKLQDVVNQNAQALNTLVKQLSSNFGAISSVLNDI
LSRLDKVEAEVQIDRLITGRLQSLQTYVTQQLIRAAEIRASANLAATKMSECVLGQSKRV
DFCGKGYHLMSFPQAAPHGVVFLHVTYVPSQERNFTTAPAICHEGKAYFPREGVFVFNG
TSWFITQRNFFSPQIITTDNTFVSGNCDVVIGIINNTVYDPLQPELDSFKEELDKYFKNHTS
PDVDLGDISGINASVVNIQKEIDRLNEVAKNLNESLIDLQELGKYEQYIKWPWYVWLGFI
AGLIAIVMVTILLCCMTSCCSCLKGACSCGSCCKFDEDDSEPVLKGVKLHYT

The invention includes a polypeptide comprising an amino acid sequence having sequence identity to SEQ ID NO: 147. The invention includes a fragment of a polypeptide comprising SEQ ID NO: 147. The invention includes a diagnostic kit comprising a polypeptide comprising SEQ ID NO: 147, or a fragment thereof. The invention includes a diagnostic kit comprising a polynucleotide sequence encoding SEQ

[redacted]

ID NO: 147, or a fragment thereof. The invention includes an immunogenic composition comprising a polypeptide comprising SEQ ID NO: 147, or a fragment thereof. The invention includes an antibody which recognizes a polypeptide comprising SEQ ID NO: 147, or a fragment thereof. SEQ ID NO: 147 demonstrates functional homology to a coronavirus spike protein.

Predicted transmembrane regions of SEQ ID NO: 147 are identified below.

Predicted Transmembrane helices of SEQ ID NO: 147

```
The sequence positions in brackets denominate the core region.
Only scores above 500 are considered significant.

Inside to outside helices :  18 found
      from         to     score center
   1 (   1)  16 (  16)     959      9
 233 ( 237) 257 ( 252)     905    244
 345 ( 347) 364 ( 361)     490    354
 345 ( 354) 369 ( 369)     420    362
 497 ( 497) 513 ( 513)     239    506
 573 ( 573) 588 ( 588)     811    580
 645 ( 648) 666 ( 663)     302    656
 690 ( 696) 714 ( 711)     428    704
 857 ( 860) 882 ( 874)    1508    867
1031 (1031)1046 (1046)     446   1039
1199 (1203)1219 (1217)    2667   1210

Outside to inside helices :  13 found
      from         to     score center
   1 (   1)  17 (  17)     684     10
 222 ( 222) 240 ( 237)     238    229
 244 ( 247) 264 ( 264)     613    254
 349 ( 355) 369 ( 369)     314    362
 496 ( 496) 511 ( 511)     488    503
 573 ( 573) 591 ( 591)     712    581
 650 ( 652) 666 ( 666)     474    659
 674 ( 679) 702 ( 696)     190    686
 691 ( 696) 713 ( 711)     210    704
 866 ( 868) 886 ( 886)    1172    876
1198 (1201)1215 (1215)    3221   1208
```

SEQ ID NO: 147, the spike protein, is a surface exposed polypeptide. Recombinant expression of a protein can be hindered by hyrophobic transmembrane regions. Accordingly, the invention includes a polypeptide comprising SEQ ID NO: 147 wherein one or more of the hydrophobic regions identified above is removed. The invention further includes a polynucleotide encoding such a polypeptide. The invention includes recombinantly expressing the protein in a host cell.

Further characterization of SEQ ID NO: 147 is set forth below.

PSORT — Prediction of Protein Localization Sites

```
version 6.4 (WWW)
MYSEQ          1255 Residues
Species classification: 4

*** Reasoning Step: 1

Preliminary Calculation of ALOM (threshold: 0.5)
     count: 2
     Position of the most N-terminal TMS: 496 at i=2
MTOP: membrane topology (Hartmann et al.)
     I(middle): 503   Charge diffirence(C-N):  1.0
McG: Examining signal sequence (McGeoch)
     Length  of  UR:   13
     Peak Value of UR:   3.28
     Net Charge of CR: 0
     Discriminant Score:      8.66
GvH: Examining signal sequence (von Heijne)
     Signal Score (-3.5): 5.94
     Possible cleavage site: 13
>>> Seems to have a cleavable N-term signal seq.
Amino Acid Composition of Predicted Mature Form:
   calculated from 14
ALOM new cnt: 1 ** thrshld changed to -2
Cleavable signal was detected in ALOM?: 0B
ALOM: finding transmembrane regions (Klein et al.)
     count: 1  value: -12.26  threshold: -2.0
     INTEGRAL    Likelihood =-12.26   Transmembrane 1202 -1218 (1194 -
1228)
     PERIPHERAL  Likelihood =  0.16
     modified ALOM score:   2.55
>>> Seems to be a Type Ia membrane protein
     The cytoplasmic tail is from 1219 to 1255 (37 Residues)
Rule: vesicular pathway
Rule: vesicular pathway
Rule: vesicular pathway
(14) or uncleavable?
Gavel: Examining the boundary of mitochondrial targeting seq.
      motif at: 14
     Uncleavable? Ipos set to: 24
Discrimination of mitochondrial target seq.:
     positive ( 2.18)
Rule: vesicular pathway
Rule: vesicular pathway
Rule: vesicular pathway

*** Reasoning Step: 2

KDEL   Count: 0
Checking apolar signal for intramitochondrial sorting
  (Gavel position 24)  from: 1  to: 10  Score:  8.0
SKL motif (signal for peroxisomal protein):
     pos: 964(1255), count: 1   SRL
     SKL score (peroxisome):  0.1
Amino Acid Composition Tendency for Peroxisome:   1.37
     AAC not from the N-term., score modified
```

```
Peroxisomal proteins?   Status: notclr
     AAC score (peroxisome): 0.079
Amino Acid Composition tendency for lysosomal proteins
   . score:  0.39  Status: notclr
GY motif in the tail of typeIa? (lysosomal)
Checking the amount of Basic Residues (nucleus)
Checking the 4 residue pattern for Nuclear Targeting
Checking the 7 residue pattern for Nuclear Targeting
Checking the Robbins & Dingwall consensus (nucleus)
Checking the RNA binding motif (nucleus or cytoplasm)
Nuclear Signal   Status: negative ( 0.00)
Type Ia is favored for plasma memb. proteins
Checking the NPXY motif..
Checking the YXRF motif..
Checking N-myristoylation..

----- Final Results -----

plasma membrane --- Certainty= 0.460(Affirmative) < succ>
microbody (peroxisome) --- Certainty= 0.171(Affirmative) < succ>
endoplasmic reticulum (membrane) --- Certainty= 0.100(Affirmative) <
succ>
endoplasmic reticulum (lumen) --- Certainty= 0.100(Affirmative) < succ>
```

SEQ ID NO: 147 appears to have a N-terminus signaling region, followed by a surface exposed region, followed by a transmembrane region followed by a C-terminus cytoplasmic domain region. Accordingly, the invention includes an immunogenic, surface exposed fragment of SEQ ID NO: 147. Preferably, said fragment comprises an amino acid sequence which does not include the last 50 amino acids of the C-terminus of SEQ ID NO: 147. Preferably, said fragment comprises an amino acid sequence which does not include the last 70 amino acids of the C-terminus of SEQ ID NO: 147. Preferably, said fragment does not include a transdomain region of SEQ ID NO: 147. Preferably, said fragment does not include a C-terminus cytoplasmic domain of SEQ ID NO: 147. Preferably, said fragment does not include a N-terminus signal sequence. Preferably, said fragment does not include amino acids 1 – 10 of the N-terminus of SEQ ID NO:147. Preferably, said fragment does not include amino acids 1 – 14 of the N-terminus of SEQ ID NO: 147.

The spike protein of coronaviruses may be cleaved into two separate chains into S1 and S2. The chains may remain associated together to form and form a dimer or a trimer. Accordingly, the invention includes a polypeptide comprising SEQ ID NO: 147 wherein said polypeptide has been cleaved into S1 and S2 domains. The invention further includes a polypeptide comprising SEQ ID NO: 147 wherein amino acids 1 – 10,

preferably amino acids 1 – 14 of the N-terminus are removed and further wherein SEQ ID NO: 147 is cleaved into S1 and S2 domains. Preferably the polypeptide is in the form of a trimer.

Predicted N-glycosylation sites of SEQ ID NO: 147 are identified below:

Prediction of N-glycosylation sites of SEQ ID NO: 147

SeqName	Position	Potential	Jury agreement	NGlyc result
SEQID 147	29 NYTQ	0.7751	(9/9)	+++
SEQID 147	65 NVTG	0.8090	(9/9)	+++
SEQID 147	109 NKSQ	0.6081	(7/9)	+
SEQID 147	119 NSTN	0.7039	(9/9)	++
SEQID 147	158 NCTF	0.5808	(7/9)	+
SEQID 147	227 NITN	0.7518	(9/9)	+++
SEQID 147	269 NGTI	0.6910	(9/9)	++
SEQID 147	318 NITN	0.6414	(9/9)	++
SEQID 147	330 NATK	0.6063	(8/9)	+
SEQID 147	357 NSTF	0.5746	(8/9)	+
SEQID 147	589 NASS	0.5778	(6/9)	+
SEQID 147	602 NCTD	0.6882	(9/9)	++
SEQID 147	699 NFSI	0.5357	(7/9)	+
SEQID 147	783 NFSQ	0.6348	(9/9)	++
SEQID 147	1080 NGTS	0.5806	(7/9)	+
SEQID 147	1116 NNTV	0.5106	(5/9)	+
SEQID 147	1176 NESL	0.6796	(9/9)	++

Accordingly, the invention includes a polypeptide comprising a fragment of SEQ ID NO: 147 wherein said fragment comprises one or more of the glycosylation sites identified above. The invention further includes a polynucleotide encoding one or more of the fragments identified above. This glycosylation site can be covalently attached to a saccharide. Accordingly, the invention includes a polypeptide comprising a fragment of SEQ ID NO: 147 wherein said fragment comprises one or more of the glycosylation sites identified above and wherein said polypeptide is glycosylated at one or more of the sites identified above.

Predicted O-glycosylation sites are identified below:

Prediction of O-glycosylation sites

Name	Residue	No.	Potential	Threshold	Assignment
SEQID 147	Thr	698	0.8922	0.7696	T
SEQID 147	Thr	706	0.9598	0.7870	T
SEQID 147	Thr	922	0.9141	0.7338	T
SEQID 147	Ser	36	0.8906	0.7264	S
SEQID 147	Ser	703	0.8412	0.7676	S

The invention includes a polypeptide comprising a fragment of SEQ ID NO: 147 wherein said fragment comprises one or more of the o-glycosylation sites identified above. The invention further includes a polynucleotide encoding one or more of the fragments identified above. The invention further includes a polypeptide comprising a fragment of SEQ ID NO: 147 wherein said fragment comprises one or more of the 0-glycosylation sites identified above and further wherein the polypeptide is covalently bonded to a saccharide at one or more of the included glycosylation sites.

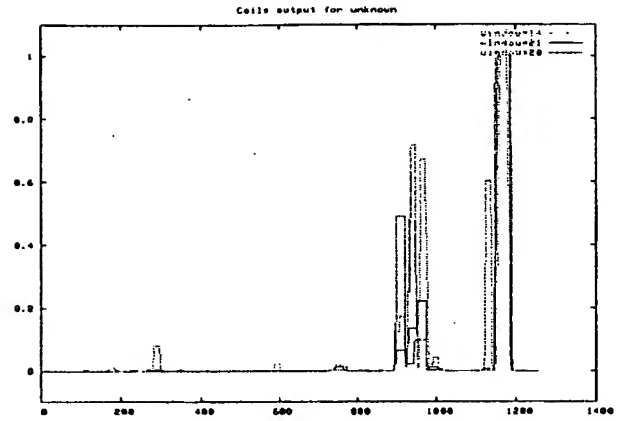
The invention further includes a polypeptide comprising a fragment of SEQ ID NO: 147 wherein said fragment comprises one or more of the N-glycosylation sites identified above and further wherein said fragment comprises one or more of the O-glycosylation sites identified above.

The invention includes a polypeptide comprising a fragment of SEQ ID NO: 147 wherein said fragment does not include one or more of the glycosylation sites identified above. The invention also includes a polynucleotide encoding such a polypeptide.

Predicted phosphorylation sites of SEQ ID NO: 147 are Ser-346, Tyr-195, and Tyr-723. Accordingly, the invention comprises a polypeptide comprising a fragment of SEQ ID NO: 147 wherein said fragment comprises at least ten amino acid residues and wherein said fragment comprises one or more of the amino acids selected from the group consisting of Ser-346, Tyr-195, and Tyr-723. In one embodiment, one or more of the amino acids selected from the group consisting of Ser-346, Tyr-195, and Tyr-723 are phosphorylated.

Predicted coiled coils of SEQ ID NO: 147 are identified below:

Coiled coil Prediction:



Accordingly, the invention comprises a polypeptide sequence comprising a fragment of SEQ ID NO: 147 wherein said fragment includes a coiled region of SEQ ID NO: 147. The invention comprises a polypeptide sequence comprising a fragment of SEQ ID NO: 147, wherein said fragment does not include a coiled region of SEQ ID NO: 147.

The ORF1a and ORF1b sequences of coronaviruses are typically translated as a single ORF1ab polyprotein. Slippage of the ribosome during translation generates an a-1 frameshift. One region of such slippage is illustrated below:

```
   gggttttacacttagaaacacagtctgtaccgtctgcggaatgtggaaaggttatggctgtagttgtga
+1   G  F  T  L  R  N  T  V  C  T  V  C  G  M  W  K  G  Y  G  C  S  C  D
+3  G  F  Y  T  -  K  H  S  L  Y  R  L  R  N  V  E  R  L  W  L  -  L  -
   ccaactccgcgaacccttgatgcagtctgcggatgcatcaacgtttttaaacgggtttgcggtgtaagt
+1   Q  L  R  E  P  L  M  Q  S  A  D  A  S  T  F  L  N  G  F  A  V  -  V
+3  P  T  P  R  T  L  D  A  V  C  G  C  I  N  V  F  K  R  V  C  G  V  S
   gcagcccgtcttacaccgtgcggcacaggcactagtactg
+1   Q  P  V  L  H  R  A  A  Q  A  L  V  L
+3  A  A  R  L  T  P  C  G  T  G  T  S  T
```

which would generate the following translational slippage:

```
ccaactccgcgaacccttgatgcagtctgcggatgcatcaacgtttttaaacgggtttgcggtgtaagt
    Q  L  R  E  P  L  M  Q  S  A  D  A  S  T  F  L  N  R  V  C  G  V  S
```

Accordingly, the invention includes a polypeptide comprising SEQ ID NO: 148. SEQ ID NO: 148 is set forth below.

SEQ ID NO: 148

```
MESLVLGVNEKTHVQLSLPVLQVRDVLVRGFGDSVEEALSEAREHLKNGTCGLVELEKGVLPQLEQPYV
FIKRSDALSTNHGHKVVELVAEMDGIQYGRSGITLGVLVPHVGETPIAYRNVLLRKNGNKGAGGHSYGI
DLKSYDLGDELGTDPIEDYEQNWNTKHGSGALRELTRELNGGAVTRYVDNNFCGPDGYPLDCIKDFLAR
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[redacted]